BCR-ABL-transformed GMP as myeloid leukemic stem cells.

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Public Summary:

Scientific Abstract:
During blast crisis of chronic myelogenous leukemia (CML), abnormal granulocyte macrophage progenitors (GMP) with nuclear beta-catenin acquire self-renewal potential and may function as leukemic stem cells (Jamieson et al. N Engl J Med, 2004). To develop a mouse model for CML-initiating GMP, we expressed p210(BCR-ABL) in an established line of E2A-knockout mouse BM cells that retain pluripotency in ex vivo culture. Expression of BCR-ABL in these cells reproducibly stimulated myeloid expansion in culture and generated leukemia-initiating cells specifically in the GMP compartment. The leukemogenic GMP displayed higher levels of beta-catenin activity than either the nontransformed GMP or the transformed nonGMP, both in culture and in transplanted mouse BM. Although E2A-deficiency may have contributed to the formation of leukemogenic GMP, restoration of E2A-function did not reverse BCR-ABL-induced transformation. These results provide further evidence that BCR-ABL-transformed GMP with abnormal beta-catenin activity can function as leukemic stem cells.

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